

# Iniencephaly and Anencephaly with Spinal Retroflexion: A Comparative Study of Twelve Human Specimens

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## Abstract

**Objective:** To study the degree of retroflexion of the cervical spine and the congenital malformations present in cases of iniencephaly and anencephaly.

**Methods:** Twelve stillborn fetuses were examined. Those with anencephaly are prefixed by AN and serially numbered from 1 to 8, and those with iniencephaly are prefixed by IN and serially numbered from 1 to 4.

The specimens were fixed in 25% formaldehyde. Anteroposterior and lateral plain x-ray of the whole body were taken four weeks after fixation. Necropsies were performed and the anomalies observed were recorded and photographed.

**Results:** According to the length of the neck and the direction of the face, retroflexion of the cervical spine was classified into severe, moderate and mild forms.

Retroflexion was severe in 2 cases (IN1, IN2), moderate in one (IN3) and mild in eight (IN4, AN1-4). The associated malformations affected most organs systems and comprised left diaphragmatic hernia in six cases, broad base of the nose in nine specimens, absent left kidney and hypoplastic lungs in two cases; Fallots tetralogy and patent foramen ovale in one case each.

**Conclusion:** The presence of cervical retroflexion and numerous similar congenital malformations justify a comparative study on twelve cases of iniencephaly and anencephaly. The appearance of the cranial cavity and the brain and the frequent occurrence of caudal myelocele in iniencephaly suggests a different time of onset of these two classes of malformation. This largely reflects the closure of the ends of the neural tube at different times.

**Keywords:** Iniencephaly, Anencephaly, Spinal retroflexion.

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## Introduction

Iniencephaly is a relatively uncommon malformation consisting of a defect in the occiput involving the foramen magnum, spina bifida of

many vertebrae, and retroflexion of the head on the spine. Since Lewis<sup>1</sup> study, Iniencephaly has been divided into two types, iniencephaly clausus and iniencephaly apertus; the latter of which has an encephalocele while the former does not.

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It has been regarded as an extreme form of the klippel-feil syndrome, <sup>2</sup> and has also been classified with anencephaly in large patient groups. <sup>3</sup> The association with anencephaly seems to have originated with Howkins and Lawrie <sup>4</sup> who included anencephalics with retroflexion and iniencephalics under one diagnostic category, iniencephaly. Coffey <sup>5</sup> felt that they are separate entities and should not be classified together. The present authors feel that there is some justification to both points of view. We agree with Coffey that the time of onset and the skull malformation are different in the two groups. However, taking into account the retroflexion of the rostral vertebrae and the associated malformations, Howkins and Lawrie's opinion can also be partly justified.

This paper attempts to present the morphological features of twelve fetuses with retroflexion of the cervical spine, which includes examples of both iniencephaly as defined by Lewis <sup>1</sup> and anencephaly with retroflexion according to Balantyne. <sup>6</sup> We will attempt to point out important correlations with respect to the associated malformation and a classification of spinal retroflexion is suggested.

### **Materials and Methods**

This study is based on gross and radiographic examination of twelve stillborn human fetuses obtained from the obstetric department of several hospitals at Amman, Jordan. A detailed obstetric history with special reference to any ailment or medication during the first trimester of pregnancy was recorded in each case. Those with anencephaly are prefixed by AN and serially numbered from 1 to 8 and those with iniencephaly are prefixed by IN and serially numbered from 1 to 4.

The specimens were fixed in 25% formaldehyde. Anteroposterior and lateral views of roentgenograms (plain x-ray) of the whole body were taken four weeks after fixation. Following the examination of external anomalies, necropsies were performed.

The anomalies observed were recorded and the pertinent photographs secured.

### **Results**

The fetuses AN1- AN8 were two males and six females and they were born to; first gravida of 17 years, sixth gravida of 32 years, fourth gravida of 30 years, first gravida of 28 years, ninth gravida of 42 years, sixth gravida of 38 years, first gravida of 22 years and second gravida of 40 years, respectively. Foetuses IN1-IN4 were two males and two females and were born to ninth gravida of 39 years, second gravida of 40 years, first gravida of 20 years and third gravida of 31 years, respectively. All fetuses were premature ranging from 28 to 36 weeks of pregnancy, and their weights range between 960 and 1850 g. in the AN group and between 750 and 1900 g. in the IN group. All deliveries were normal, pregnancy was complicated by polyhydramnios in AN1, AN5 and AN8 and by Pre-eclamptic toxemia in AN8, IN1 and IN2. In all cases, there was no history of drug intake during the first trimester except for Ferrous gluconate and folic acid during the second trimester. Survival ranged from few hours to a maximum of three days.

The twelve cases with retroflexion of the cervical spine were found to represent two diagnostic entities. Four (IN1-IN4) are examples of iniencephaly apertus while eight (AN1-AN8) had anencephaly with retroflexion. <sup>6</sup> There were no examples of the third type, iniencephaly clauses. <sup>1</sup> Figures (1-10) illustrate the above type of cases.

Two specimens with iniencephaly apertus and four with anencephaly had anterior spina bifida (fig.11) and although the central nervous system was not extensively examined as part of this study, both specimens with iniencephaly had increased the size of both of the lateral ventricles. Malformations found in the twelve specimens are listed in table (1). These affected most of the major organs and comprised left posterior diaphragmatic hernia in six cases (IN2, IN4, AN4-7), absent neck in all specimens and broad base of nose in nine specimens including all cases

of iniencephaly, absent left kidney in one specimen of iniencephaly and two specimens of anencephaly. In addition, hypoplastic lungs were seen in one specimen of anencephaly. Cardiovascular malformations was found in two specimens (IN2 and AN3) Figures (12,13), urinary tract malformations in three specimens (IN3, AN4 and AN5) and gastro-intestinal malformations in three specimens (IN1, IN4, AN3). Bilateral club foot was seen in two cases of iniencephaly (IN1, IN4) and in four cases of anencephaly (AN2, AN6-8).

Careful examination of the cases presented in this study suggests that the retroflexion of the cervical spine can be divided into; severe, moderate and mild forms. In the severe form (fig. 1,2) the neck is absent, the face looks upward, the mentothoracic junction is convex, the hairline extends on the back to the lumbar region, the cervical and upper thoracic vertebrae are drastically reduced in number, anterior spina bifida is frequent and a diaphragmatic defect is present. In the moderate retroflexion (fig. 3,4), the neck is very short, the face looks upward and forward at an angle of about 45° with the horizontal plane, the mentothoracic junction is flat, the hairline extends on the back to the midthoracic level, anterior spina bifida and diaphragmatic defect are often present. In the mild form of cervical retroflexion, the neck is short, the face looks more or less forward, the mentothoracic junction is marked by a shallow groove, the hairline extends on the back to the lower cervical region, anterior spina bifida and diaphragmatic defects are absent. One of the mild forms of cervical retroflexion was iniencephaly (IN4) (fig. 5,6), and the rest were cases of anencephaly (AN1-An8) (fig. 7,8,9,10). Among the specimens studied in the present work, cervical retroflexion was severe in two cases (IN1, IN2), moderate in one (IN3) and mild in eight (IN4, AN1-8).



**Fig. 1: Anterior view of IN<sub>1</sub> showing severe cervical retroflexion and convex mentothoracic junction.**



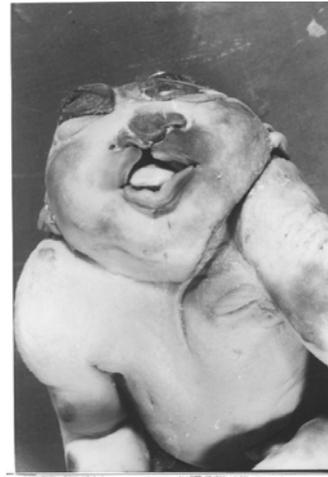
**Fig. 2: Posterior view of IN<sub>1</sub> showing a hairline that extends to the lumbar region.**



**Fig. 3: Anterior view of IN<sub>3</sub> showing moderate cervical retroflexion and flat mentothoracic junction.**



**Fig. 4:** Posterior view of IN<sub>3</sub> showing a hairline that extends to the midthoracic region.



**Fig. 7:** Anterior view of AN<sub>2</sub> showing mild form of cervical retroflexion and a median cleft lip.



**Fig. 5:** Anterior view of IN<sub>4</sub> showing mild cervical retroflexion. The neck is short and the face looks more or less forward.



**Fig. 8:** Posterior view of AN<sub>2</sub> showing craniorachischisis.



**Fig. 6:** Posterior view of IN<sub>4</sub> showing a hairline that extends on the back to the lower cervical region.



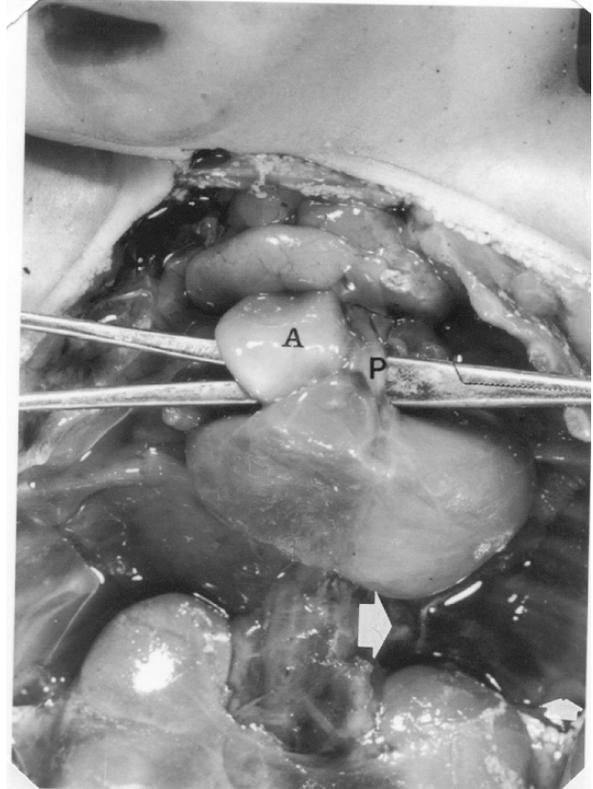
**Fig. 9:** Anterior view of AN<sub>1</sub> showing low set ears, broad base nose and ridged palate.



**Fig. 10:** *Posterior view of AN<sub>1</sub> showing a mild degree of cervical rachischisis.*



**Fig. 11:** *Radiograph (anteroposterior view) showing distorted cervical vertebrae and anterior spina bifida (arrow).*



**Fig. 12:** *Anterior view of the heart and great vessels of AN<sub>3</sub> showing some of the features of Fallot's tetralogy. The pulmonary artery (p) is narrowed while the aorta (A) is enlarged. Arrows point at the site of a diaphragmatic hernia.*



**Fig. 13:** *Part of the heart of IN<sub>2</sub> showing a large foramen oval (arrow) sp = septum primum.*

**Table 1: Associated malformations in twelve fetuses with spinal retroflexion.**

<b>Location</b>	<b>IN1</b>	<b>IN2</b>	<b>IN3</b>	<b>IN4</b>	<b>AN1</b>	<b>AN2</b>	<b>AN3</b>	<b>AN4</b>	<b>AN5</b>	<b>AN6</b>	<b>AN7</b>	<b>AN8</b>
<b>Head/Ears</b>	N	Low set	Low set	N	Low set	Low set	Low set	Low set	Low set	Low set	N	N
<b>Nose</b>	Broad base	Broad base	Broad base	Broad base	Broad base	N	N	Broad base	N	Broad base	Broad base	Broad base
<b>Mouth/Jaw</b>	N	N	N	N	Ridged palate	Cleft lip & palate	N	N	Cleft lip	N	N	N
<b>Neck</b>	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
<b>Diaphragm</b>	Hernia	Hernia	N	Eventration	Hernia	Hernia	N	N	Hernia	N	N	N
<b>Respiratory</b>	Incomplete lobation of lung	Incomplete lobation	N	N	Incomplete lobation	N	Hypoplastic lungs	N	N	Incomplete lobation	N	N
<b>Cardio-vascular</b>	N	Patent foramen orale	N	N	N	N	Fallots tetralogy	N	N	N	N	N
<b>Urinary tract</b>	N	N	Absent Kidney	N	N	N	N	Absent Kidney	Absent Kidney	N	N	N
<b>Gastro-intestinal</b>	Cecum in left upper quadrant	N	N	Cecum in right upper quadrant	N	N	Short oesophagus	N	N	N	N	N
<b>Spine anterior spina bifida</b>	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	No
<b>Rachischisis</b>	Club foot	N	N	Club foot	N	Club foot	N	N	N	Club foot	Club foot	Club foot
<b>Meningocele</b>	Yes	No	No	No	No	No	No	No	No	No	No	No
<b>Legs</b>	No	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes

*N = Normal*

## **Discussion**

The important distinction between anencephaly with spinal retroflexion and iniencephaly clausus or apertus, that is related to the time of onset.<sup>7</sup> The former in which cranial nervous tissue is directly exposed to the surface, arises prior to closure of the cephalic neural folds in 24 days gestational age.<sup>8</sup> In contrast, cranial malformations with uninterrupted skin covering, such as iniencephaly, arise after the cephalic neural tube has closed. The development of a membranous neurocranium is dependent on this fusion. Morphologically, the most prominent and characteristic feature of iniencephaly is hyperextension of the neck so that the face looks upward. Since this feature is sometimes found in the anencephalics, the argument of Lemire<sup>1</sup> that includes such cases in the group of iniencephaly, seems justified. However, the term 'spinal retroflexion', since its first proposal by Howkins and Lawrie,<sup>4</sup> has been used rather inaccurately.

Anencephalics with a mild degree of cervical retroflexion<sup>7</sup> have also been classified with iniencephaly as both have certain degree of retroflexion. Relaxation of the criterion of retroflexion to this extent may prompt merger of a greater proportion of anencephalics in iniencephaly as both have certain degree of retroflexion. Therefore, it is desirable that the hallmarks of spinal retroflexion should be laid down and different degrees of retroflexion discriminated.

According to the present findings, retroflexion of the cervical spine was conveniently described in severe, moderate and mild forms. Obviously, the degree of cervical retroflexion, severity of spinal deformity and the incidence of associated visceral anomalies (of which the posterior diaphragmatic defect is most obvious and easily recognized) all go together and help for proper classification.<sup>9</sup>

Since anencephaly and iniencephaly are lethal malformations, the presence in some cases of other malformations does not seem to have attracted much interest.<sup>10-12</sup> In the present study most of the specimens displayed major malformation of one or more systems. The thorax has frequently been noted to have major malformations affecting the cardiac septa and lobation of the lung,<sup>6,13</sup> similar developmental defects were observed in the present study. Diaphragmatic defects occurred in six of our specimens and in many previously reported ones.<sup>14-17,11</sup> Association with diaphragmatic defects is another feature common to retroflexion of the anencephalic and iniencephalic types. Its pathogenesis and high correlation with cervical retroflexion has not been explained to our knowledge.

Because of these associated malformations characteristics, specimens with anencephaly and retroflexion of the rostral spine can be legitimately discussed within the morphological, though not etiological, spectrum of iniencephaly. For the purposes of genetic counseling, iniencephaly seems to be treated as a neural tube defect.<sup>11</sup>

The obstetric history of the examined cases does not seem to have contributed to the etiology or epidemiology of the studied anomalies, however, the presence of the associated defects indicates that neural tube defects are epidemiologically and probably etiologically heterogeneous.<sup>18,19</sup>

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## الجنين قفوي الدماغ والجنين عديم الدماغ: دراسة مقارنة لاثني عشر جنينا آدميا

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### الملخص:

### الهدف:

دراسة مستوى الانحناء الى الخلف في المنطقة العنقية من العمود الفقري والتشوهات الخلقية الموجودة في حالات الجنين قفوي الدماغ والجنين عديم الدماغ.

### الطرق:

استخدم في هذا البحث اثنا عشر طفلا ولدوا متوفين، وقد رمزنا للطفل عديم الدماغ بالرمز AN واشرنا إليهم بالارقام من 1-8، بينما رمزنا للطفل قفوي الدماغ بالرمز IN واشرنا إليهم بالارقام من 1-4. تم تخنيط الجثث بمحلول الفورمالدهايد 25% ثم أخذت صور شعاعية: منظر امامي ومنظر جانبي بعد التخنيط بأربعة أسابيع. تم تشريح الجثث وقمنا بتسجيل وتصوير التشوهات الخلقية.

### النتائج:

تم تصنيف الانحناء في المنطقة العنقية الى ثلاث درجات: شديد الانحناء ومتوسط الانحناء وقليل الانحناء ولوحظ انحناء شديد في الأجنة IN1 وIN2 وانحناء متوسط في الجنين IN3 وانحناء قليل في الجنين IN4 والأجنة AN1-4، وبالنسبة للتشوهات الخلقية وجدنا فتقاً في الناحية اليسرى من الحجاب الحاجز في ست حالات وأنفاً ذا بداية عريضة في تسع حالات، وغياب الكلية اليسرى في حالة وضمور الرئتين في حالة، وكذلك وجود رباعي فالوت في حالة ووجود فتحة في الحاجز الأذيني في حالة واحدة.

### الاستنتاج:

إن وجود انحناء الى الخلف في المنطقة العنقية وعدة تشوهات خلقية متشابهة يدعو الى إجراء مقارنة في اثني عشرة حالة من الجنين قفوي الدماغ والجنين عديم الدماغ، وإن الشكل الخارجي لتجويف الجمجمة والدماغ مع وجود فتق في الحبل الشوكي في الجنين قفوي الدماغ يشير الى ان هذه التشوهات تكونت في مراحل مختلفة من عمر الجنين، وهي تعكس الى حد كبير إغلاق طرف القناة العصبية في اوقات مختلفة.

### الكلمات الدالة:

الجنين قفوي الدماغ، الجنين عديم الدماغ، الانحناء للخلف في المنطقة العنقية من العمود الفقري.